REMARKS:

Claims 1-25 are in the case and presented for consideration.

The Applicants thank the Examiner for examining all of the claims.

Claim 1 has been amended to eliminate the objectionable language concerning "derivatives" and two Terminal Disclaimers are filed with this amendment to address the Examiner's provisional double patenting rejection.

In reply to the Examiner's rejection of the claims as being obvious under 35 U.S.C. 103 from the stated combination of the Mckeage et al. article with four U.S. patents and the Swarbrick Encyclopedia of Pharmaceutical Technology page 121, please consider the following observations.

When assessing whether a technical solution is or is not obvious from the prior art, two items should be taken into consideration, i.e.

(i) the technical problem to be solved; and

(ii) the technical solution by which the inventors solve such technical problem.

A technical solution might be found to be obvious only after there are, in the prior art, some hints directing the person skilled in the art to the technical solution, these hints being connected to the technical problem to be solved.

The technical problem to be solved by the present application is clearly explained in the bridge paragraph of pages 1 and 2 that reads:

> "The tetravalent platinum complexes, nevertheless, are generally almost insoluble in water (about 0.03 g/100 g), have small bulk density of about 0.2 g/ml, small tap density of about 0.4 g/ml and extremely high electrostatic charge. These physical properties represent a significant problem for preparation of a solid pharmaceutical composition. In addition, tetravalent platinum complexes are chemically unstable when in contact with metals or many commonly used pharmaceutical excipients; this fact reduces the stability of the active substance in the pharmaceutical composition."

In other words, there was a need for a chemically stable pharmaceutical composition comprising a tetravalent platinum complex as the active ingredient or matter, but without having the above mentioned undesired properties which basic composition should be used as such or further processed to another medicament form.

The inventors of the subject application solved the above defined technical problem by proposing the solution of Claim 1 of the present application, i.e. implementing wet granulation of a mixture of platinum complex of a tetravalent platinum wetted by water, at least one neutral saccharide and at least one native and/or modified polysaccharide (hereafter called "the present excipients") to obtain a granulate with particles smaller than 0.5 mm. The principle of this solution is the common wet granulation of all the mentioned components together (hereafter called "common wet granulation") to reach the granulate

with the defined particle size.

The cited prior art can be divided into the following group as to their relevance:

(1) Document mentioning neither the common wet granulation nor the present excipients: U.S. Patent 6,503,943 to Zak. This document has no relevance in view of the present solution since it does not hint at any feature of the Claim 1.

(2) Documents mentioning the present excipients but being silent on the common wet granulation: The Mckeage article; U.S. Patent 5,256,653 to Keppler; and U.S. Patent 5,900,252 to Calanchi. It is evident that these documents themselves (i.e. considered separately without combining them with a further prior art document) have no relevance in view of the present solution since they do not provide any hint concerning the common wet granulation to complete the present solution.

(3) Document mentioning both the present excipients and a granulation: U.S. Patent 6,221,393 to Collaueri; and Swarbrick Encyclopedia of Pharmaceutical Technology.

(3a) The present solution could not have been derived from neither U.S. Patent 6,221,393 itself or its combination with any document of the groups (1) and/or (2) for the reasons that:

(i) U.S. Patent 6,221,393 is focused to hydrophilic xanthan gums (polysaccharides) having quite different properties than those of the polysaccharides used according to the present solution as a result of which these xanthan gums could not serve, for the present invetors, as a consistent model of the polysaccharide as used by them.

(ii) U.S. Patent 6,221,393 does not mention at all the tetravalent platinum complexes so that the active matters that are mentioned in U.S.

Patent 6,221,393 and have different properties from those of the tetravalent platinum complexes could not serve, for the present inventors, as a consistent model of the tetravatent platinum complexes as used by them.

(iii) U.S. Patent 6,221,393 does not concern the common wet granulation but concerns a wet granulation wherein **the excipents are granulated in absence of the active matter, i.e. <u>separately</u> from the active matter** and only after mixed with the active matter to tablet the resulting mixture. This is a considerable difference from the present solution wherein it is just the common wet granulation of the excipents together with the active matter which ensures the desired stability and properties of the active matter. All the mean particle sizes mentioned in U.S. Patent 6,221,393 are thus only related to particle size of the pregranulated polysaccharide rather than granules comprising all the components of the composition, inclusive of active matter.

(3b) The Encyclopedia of Pharmaceutical Technology only provides a general definition of the granulation not comprising any specific hint related to the technical problem to be solved by the claimed invention. Taking into account that the tetravalent platinum complexes are known to be very chemically unstable in the presence of many commonly used pharmaceutical excipients, it could not be predicted how said complexes would behave in the presence of the excipients under relatively severe wet granulation conditions (hydrolysis, mechanical energy forwarded to the granulation system) and if such granulation will eliminate the technical problem to be solved. In this point, the Encyclopedia of Pharmaceutical

Technology provides no instruction that could be exploited when working toward the claimed solution. As to the particle size itself as mentioned in the Encyclopedia of Pharmaceutical Technology, it should be stressed that the particle size smaller than 0.5 mm as used in the present solution should not be considered separately but should only be considered in combination with the present excipient and the present wet granulation representing, two further obligatory features of the present solution.

To summarize, the reasons the Examiner's obviousness objections as respectfully traversed, are that even when those with ordinary skill in the art read the cited prior art and know pharmaceutical compositions comprising the tetravalent platinum complexes in combination with neutral saccharides and polysaccharides (powder mixtures, solutions) and even when the prior art contains the technical problems being related to such compositions, despite that, the prior art contains for teaching or instructions that, comprehensibly joined, together would be able to guide the person skilled in the art to the claimed solution which is believed to represent patentable progress over the prior art.

The term "comprehensibly" should here be understood to at least require the particular instructions present in the different references toward solving a technical problem which is identical or at least equivalent to the problem solved by the combined reference. The combination of cited documents either solve different problems from that solved by the present solution or their technical problem is foggy as a result of which the particular instructions of the cited documents are far from each other to such an extent that they can not be combined to meet the invention of Claim 1 in an obvious manner to those with ordinary skill in the art without first reading the present application.

The dependent composition claims 2 to 11 and 20 to 25 are likewise believed to further distinguish the invention over the prior art.

The method claims 12 to 19 are also believed to be unobvious, since the above arguments are material for both the composition and the method of the invention. In this connection it is stressed that wet mixing the active substance with the pharmaceutical vehicles and dispersing the mixture into capsules as allegedly taught by Keppler should not be confused with the wet granulation of the present solution.

Accordingly the application and claims are believed to be in condition for allowance and favorable action is respectfully requested.

The Examiner is respectfully invited to telephone the undersigned in order to further expedite the prosecution of this application as needed.

Respectfully submitted,

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